

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions and listings of claims in the application:

1. (Currently Amended) A method of treating a subject diagnosed as having a lysosomal storage disease comprising first administering a gene therapy vector encoding a lysosomal hydrolase under the control of at least one tissue specific regulatory element and then administering **[1:]**

[(a)] an exogenously produced natural or recombinant lysosomal hydrolase **[1:]**

~~(b) — a small molecule capable of treating a lysosomal storage disease,~~
or

~~(c) — both (a) and (b),~~

such that the lysosomal storage disease is treated.

2. (Cancelled)

3. (Original) The method of claim 1, where the tissue specific regulatory element is chosen from at least one of a tissue specific promoter and a tissue specific enhancer.

4. (Original) The method of claim 1, where administering the gene therapy vector encoding a lysosomal hydrolase induces immunological tolerance to the lysosomal hydrolase.

5. (Cancelled)

6. (Currently Amended) The method of claim **[[5]] 1**, where the a lesser amount of the exogenously produced natural or recombinant lysosomal hydrolase is administered to the subject to treat the lysosomal storage disease is less than the amount than would be administered if the subject had to treat a subject with a lysosomal storage disease that has not been administered a gene therapy vector

encoding a lysosomal hydrolase or had [[has]] been administered a gene therapy vector without a tissue specific promoter controlling expression of the lysosomal hydrolase.

7. (Original) The method of claim 1, where the lysosomal storage disease is Fabry disease.

8. (Original) The method of claim 7, where the treatment results in a decrease in GL-3 in the subject compared to the GL-3 level in the subject before treatment.

9. (Original) The method of claim 7, where the lysosomal hydrolase is α -galactosidase A.

10. (Withdrawn) The method of claim 1, where the lysosomal storage disease is Pompe disease.

11. (Withdrawn) The method of claim 10, where the treatment results in a decrease in glycogen in the subject compared to the glycogen level in the subject before treatment.

12. (Withdrawn) The method of claim 10, where the lysosomal hydrolase is α -glucosidase.

13. (Original) The method of claim 1, where the gene therapy vector is a viral vector.

14. (Currently Amended) The method of claim [[11]] 13, where the viral vector is chosen from AAV1, AAV2, AAV5, AAV7₁ and AAV8.

15. (Original) The method of claim 1, where the tissue specific regulatory element is a liver specific promoter.

16. (Original) The method of claim 15, where the liver specific promoter is a human serum albumin promoter.

17. (Original) The method of claim 1, where tissue specific regulatory element is a tissue specific enhancer.

18. (Original) The method of claim 17, where the tissue specific enhancer is a human prothrombin enhancer.

19. (Withdrawn - Currently Amended) The method of claim 1, where the small molecule capable of treating a lysosomal storage disease is chosen from deoxynojirimycin, *N*-propyldeoxynojirimycin, *N*-butyldeoxynojirimycin, *N*-butyldeoxygalactonojirimycin, *N*-pentyldeoxynojirimycin ***N*-pentyldeoxynojirimycin**, *N*-heptyldeoxynojirimycin, *N*-pentanoyldeoxynojirimycin, *N*-(5-adamantane-1-ylmethoxy)pentyl-deoxynojirimycin, *N*-(5-cholesteroxypentyl)-deoxynojirimycin, *N*-(4-adamantanemethanylethylcarboxy-1-oxo)-deoxynojirimycin, *N*-(4-adamantanylethylcarboxy-1-oxo)-deoxynojirimycin, *N*-(4-phenanthrylcarboxy-1-oxo)-deoxynojirimycin, ***N*-(4-phenanthrylcarboxy-1-oxo)-deoxynojirimycin**, *N*-(4-cholesterylcarboxy-1-oxo)-deoxynojirimycin, or *N*-(4-cholestanylcarboxy-1-oxo)-deoxynojirimycin, D-threo-1-phenyl-2-palmitoylamino-3-pyrrolidino-1-propanol (P4), D-threo-4'-hydroxy-1-phenyl-2-palmitoylamino-3-pyrrolidino-1-propanol (4'-hydroxy-P4), D-threo-1-(3',4'-trimethylenedioxy)phenyl-2-palmitoylamino-3-pyrrolidino-1-propanol (trimethylenedioxy-P4), D-threo-1-(3',4'-methylenedioxy)phenyl-2-palmitoylamino-3-pyrrolidino-1-propanol (methylenedioxy-P4) and D-threo-1-(3',4'-ethylenedioxy)phenyl-2-palmitoylamino-3-pyrrolidino-1-propanol (ethylenedioxy-P4 or D-t-et-P4).

20. (Currently Amended) A method of treating a subject diagnosed as having Fabry disease comprising **first** administering a gene therapy vector encoding α -galactosidase A under the control of a human albumin promoter and 2 copies of a human prothrombin enhancer and **then** administering **[(a)]**

[(a)] an exogenously produced natural or recombinant α -galactosidase A

[(b)]

(b) — a small molecule capable of treating Fabry disease, or

(c) — both (a) and (b),

such that the Fabry disease is treated.

21. (Cancelled)

22. (Withdrawn – Currently Amended) A method of treating a subject diagnosed as having Pompe disease comprising first administering a gene therapy vector encoding α -glucosidase under the control of a liver specific promoter and optionally, at least one copy of a tissue specific enhancer, and then administering followed by administration of:

[(a)] an exogenously produced natural or recombinant α -glucosidase [(c)]

~~(b) a small molecule capable of treating Pompe disease, or~~

~~(c) both (a) and (b),~~

such that the Pompe disease is treated.

23-35. (Cancelled)

36. (New) The method of claim 20, where administering the gene therapy vector encoding a lysosomal hydrolase induces immunological tolerance to the lysosomal hydrolase.

37. (New) The method of claim 20, where a lesser amount of the exogenously produced natural or recombinant lysosomal hydrolase is administered to the subject to treat the lysosomal storage disease than would be administered if the subject had not been administered a gene therapy vector encoding a lysosomal hydrolase or had been administered a gene therapy vector without a tissue specific promoter controlling expression of the lysosomal hydrolase.

38. (New) The method of claim 20, where the treatment results in a decrease in GL-3 in the subject compared to the GL-3 level in the subject before treatment.

39. (New) The method of claim 20, where the gene therapy vector is a viral vector.

40. (New) The method of claim 39, where the viral vector is chosen from AAV1, AAV2, AAV5, AAV7, and AAV8.